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09/629,469	07/28/2000	Toshio Ota	084335-0123	3856

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EXAMINER	
SMITH, CAROLYN L	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/629,469	OTA ET AL.	
	Examin r	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2003 and 24 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,7,9,10,14,16,17 and 19-45* is/are pending in the application.

4a) Of the above claim(s) *1,6,7,9,10,14,16,17 and 19-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-45* is/are rejected.

7)☒ Claim(s) *24,25 and 28* is/are objected to.

8)☒ Claim(s) *1,6,7,9,10,14,16,17 and 19-45* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *09302003*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendments and remarks, filed 10/24/03 and 09/08/03, are acknowledged. New claims 36-45 and amended claims 24-25 and 28-35, filed 9/8/03, are acknowledged. Amended claims 29-33, 36, 38, 40-42, and 44-45, filed 10/24/03, are acknowledged.

Applicant's arguments, filed 10/24/03 and 09/08/03, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The information disclosure statement (IDS), filed 9/30/03, has been considered. It appears that the reference submitted in the 12/26/01 IDS as Maruyama et al. is now being referred to in the 9/30/03 IDS as Sugano et al. (same reference). Since this reference has a translated copy in English, it has been considered.

Claims 24-45 are herein under examination.

Claim Objection

Claims 24, 25, and 28 are objected to because of the following minor informality: Claims 24, 25, and 28 recite improper uses of a period. Correction is suggested by amending the period after SEQ ID NO to a colon.

Appropriate correction is suggested. These objections are necessitated by amendment.

Claims Rejected Under 35 U.S.C. § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The rejection of claims 24-35 is maintained and newly applied to claims 36-45 under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

This rejection is maintained and reiterated below for reasons of record.

These claimed primer sets, polynucleotides, vectors, transformants, oligonucleotides, and antisense polynucleotides are not supported by a substantial utility, because no substantial utility has been adequately established for the claimed subject matter. SEQ ID NO: 702, 6223, 10847, and 10848 may be involved in the asserted protein functions, such as those described in pages 216-241, but the mere fact that these are only asserted functions supports the notion that further research would be required to confirm a "real world" context of use.

Applicants state the elected sequences are "described as making it possible to encode a membrane or secretory protein" and both "are associated with diabetes". These statements are unpersuasive as they are assertions without factual support. The specification states using homology searches of selected clones (specification, page 216, line 9). The specification discusses the top hit data of such clones that "were predicted to encode a protein belonging to any of the categories, [such as] secretory or membrane protein" (specification, page 216, lines 22-31). The specification states some clones have relatively high homology with known proteins or genes in the same category, while others have low homology with the known proteins in the same category. This high degree of variation of homology and the idea of being in a certain

category would discourage one of skill in the art from soundly concluding that a protein belonged to any particular category without further experimentation to support these assertions. On page 216, last paragraph, of the specification, there is a list of keywords that are commonly found in the top hit data of SwissProt and GenBank. Scientific experimental data, not merely the presence of keywords, are what provides sound scientific reasoning as to whether a sequence belongs to a particular group. It is noted that a sequence with one misclassified keyword could have a cumulative erroneous effect on other sequences that were also given that keyword due to sequence similarity with the original sequence. Applicants further state HEMBA1004850, a clone containing SEQ ID NO: 706 and SEQ ID NO: 6223 was elevated in endothelial cells in a glycated protein specific manner which is believed to cause a variety of chronic diabetic complications. This is found unpersuasive as this belief is an assertion without factual support. Further scientific evidence is needed to give support to these assertions to confirm that a readily available utility exists. For example, evidence showing a significant difference between the elevation in expression level of the diseased material versus control would support the assertions made above by Applicants.

Applicants should explicitly identify a specific, substantial, and credible utility for the claimed invention and establish a probative relation between any evidence of record and the originally disclosed properties of the claimed invention.

Due to a lack of either an art recognized or alleged well established utility, the instant invention has been rejected due to also lacking the required combination of a specific, substantial, and credible utility. Although it may be credible that the polynucleotides involved in the claimed primer sets, polynucleotides, vectors, transformants, oligonucleotides, and antisense

polynucleotides may have an important function, the lack of substantial utility, as explained above, sufficiently supports this rejection.

Applicants state that the evidence or explanation of record fails to address the credibility of these specific and substantial utilities. This is found unpersuasive as the reasoning for the lack of a substantial utility is described, supra. As there does not appear to be a well-established utility for this invention, criteria must be met to fulfill specific, substantial, and credible utility.

It is noted that applicant has conducted homology studies (via BLAST, page 2 lines 30-32 and 39-48) to sequences which are known in the prior art and which has a stated sequence similarity or dissimilarity to the claimed sequence to identify predictive functions. Absent factual evidence, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject matter would be the same as that of the similar sequence. Furthermore, it is unclear whether the similar sequence identified in the prior art has actually been tested for the biological activity or whether this also is an asserted biological activity based upon sequence similarity to yet a different sequence. Note that it would have been well known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been well known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the

relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Lopez et al. (Molecular Biology, 32:881-891,1999); Attwood (Science, 290:471-473, 2000); Gerhold et al. (BioEssays, 18(12):973-981, 1996); Wells et al. (Journal of Leukocyte Biology, 61(5):545-550, 1997); and Russell et al. (Journal of Molecular Biology, 244:332-350, 1994). However, this level of factual evidence is absent here.

Claim Rejections – 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of the skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF ENABLEMENT

The rejection of claims 24-35 is maintained and newly applied to claims 36-45 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention.

Since the claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above (refer to the 35 U.S.C. § 101 rejection), one skilled in the art would not know how to use the claimed invention.

Additional evidence supporting the assertions made by Applicants in the 35 USC 101 rebuttal may overcome this enablement rejection, if a substantial utility is adequately supported by additional evidence regarding the significant expression change differences between diseased and normal genes. This rejection is maintained and necessitated by amendment.

Claims Rejected Under 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF WRITTEN DESCRIPTION

Claims 28, 34, 35, 37, 39, 41, 43, and 45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

The specification does not appear to support for "secretory or membrane protein associated with diabetes" as stated in claim 28 (lines 10, 14, and 17). Written basis is provided for "non-enzymatic protein glycation reaction is believed to be a cause for a variety of chronic diabetes complications" (page 156, second paragraph) and "genes associated with diabetes" (page 157, second paragraph), but not for a "secretory or membrane protein associated with diabetes" as stated in newly amended claim 28, which differs in scope. Because the introduction of "secretory or membrane protein associated with diabetes" lacks written basis for amended claim 28, as filed on 10/24/03, it is considered NEW MATTER. Claims 34, 35, 37, 39, 41, 43, and 45 are also rejected due to their direct, indirect or other type of involvement with claim 28. This rejection is necessitated by amendment.

FURTHER LACK OF WRITTEN DESCRIPTION

The rejection of claims 24-35 is maintained and newly applied to claims 36-45 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

The specification discloses SEQ ID NO: 702, 6223, 10847, and 10848 which correspond to nucleic acid sequences of isolated cDNA. SEQ ID NO: 702, 6223, 10847, and 10848 and their full-length complements meet the written description provisions of 35 U.S.C. 112, first paragraph. However, claims 24-45 are directed to encompass fragments and oligonucleotides (claims 24, 25, 34) as well as recited percentages of identity (claim 28) and hybridization to sequences (claim 28) which do not meet the written description provision of 35 USC 112, first

paragraph. Sequences encompassed in the claim phrases " fragment of the nucleotide sequence" (amended claim 24 and 34), "the primer set" (claim 26), "the coding region of the polynucleotide" (claim 27), "comprising a coding region of the nucleotide sequence" (claim 28), "comprising a nucleotide sequence encoding a protein comprising the amino acid sequence" (claim 28, lines 5-6 and 7-8), "the amino acid sequences" (claim 28), "up to 5% of the amino acids are substituted, deleted, inserted, and/or added" (claim 28), "the nucleotide sequence (claim 28, line 12), "comprises a nucleotide sequence encoding a protein comprising a secretory or membrane protein associated with diabetes" (claim 28, lines 13-14) , "the polynucleotide" (claims 35-39 and 42-43), "the vector" (claims 40-41 and 44-45) which do not meet the written description provision of 35 U.S.C. 112, first paragraph. Please note the "95% identity" as recited in claim 28 (line 15), could also contain sequences including the entire sequence of SEQ ID NO: 10847 plus up to 5% of additional sequence on either end of SEQ ID NO: 10847 which fails to meet the written description provision of 35 U.S.C. 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by these claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 702, 6223, 10847, and 10848, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only SEQ ID NO: 702, 6223, 10847, and 10848 and their full length complements, but not the full breadth of the claims 24-45 meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicants are reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

This rejection is maintained and necessitated by amendment.

Applicants have made some amendments which addressed some, but not all, of the written description issues mentioned above. For example, some of the fragments and additional sequence encompassed by the previous claims that lacked written description (i.e. "70% identical", "functionally equivalent", and "partial") no longer exist due to the removal of these phrases from the claims. However, the amendments do not address the remainder of the rejections listed above and are therefore insufficient to overcome the written description rejection.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28, 34, 37, 39, and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. This rejection is necessitated by amendment.

Claim 28 recites the phrase "associated with diabetes" (lines 10, 14, and 17) that is vague and indefinite. It is unclear what criteria and to what degree such association must be met so that such association is considered to have occurred. One interpretation is that something is actually part of the diabetes condition. For example, one may suppose that diabetes mellitus is present which is characterized as "a variable disorder of carbohydrate metabolism caused by a combination of hereditary and environmental factors and usually characterized by inadequate secretion or utilization of insulin, by excessive urine production, by excessive amounts of sugar in the blood and urine, and by thirst, hunger, and loss of weight" (Merriam Webster online dictionary). A direct association with this type of diabetes would be excessive amounts of sugar in the blood and urine. Another interpretation of this phrase is that something occurs at the same time as diabetes, but is not an actual condition of diabetes. Therefore, clarification of this vague and indefinite issue via clearer claim wording is requested. Claims 34, 37, 39, and 43 are also rejected due to their dependency from claim 28.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 28 and 34-35 is maintained and newly applied to 37, 39, 41, 43, and 45 under 35 U.S.C. 102(e)(2) as being anticipated by Shin et al. (P/N 6,291,645).

This rejection is maintained and reiterated for reasons of record.

As the coding region of SEQ ID NO: 10847 consists of residues 416-1174, Shin et al. disclose a sequence (SEQ ID NO: 8, residues 2599-2620) including a 22-mer which matches residues 767-788 of SEQ ID NO: 10847 in the instant invention, as stated in claim 28. Shin et al. disclose the sequence of SEQ ID NO: 8 (col. 79-86) encodes an amino acid sequence of a p160 polypeptide (col. 8, lines 51-57). Shin et al. disclose recombinant expression vectors containing nucleic acid molecules of the invention, host cells which contain the recombinant expression vectors, and nucleic acids which are antisense to the nucleic acid molecules described in the invention (abstract and col. 5, lines 24-30).

Thus, Shin et al. anticipate the limitations of claims 28, 34-35, 37, 39, 41, 43, and 45.

Applicants ask that the scope of the present claims be assessed. It is noted that part (a) of instant claim 28 "comprises a coding region" which can be broadly and reasonably interpreted to

mean a section or the entire coding region. Shin et al. disclose a polynucleotide comprising a section of the coding region of SEQ ID NO: 10848 and thus anticipate instant claim 28.

This rejection is maintained for claims 28 and 34-35 and necessitated by amendment for claims 37, 39, 41, 43, and 45.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and

1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

December 30, 2003

ARDIN H. MARSCHEL
PRIMARY EXAMINER